Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) A method of screening a substance of interest for heme independent ~~inhibition~~ modulation of enzymatic activity of soluble guanylyl cyclase (sGC) comprising:

a) obtaining purified $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme or a cell lysate containing $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme;

b) assaying said purified enzyme or cell lysate for formation of cGMP from GTP in the presence of said substance;

c) assaying said purified enzyme or cell lysate for formation of cGMP from GTP in the absence of said substance;

optionally, d) ~~optionally,~~ carrying out steps b) and c) in the presence ~~or absence~~ of an activator other than said substance; ~~and~~

e) comparing the results from b) and c), and, d), if present, to ~~determine whether~~ yield a comparison result; and

f) assessing the ability of said substance ~~inhibits~~ to modulate cGMP production by said purified enzyme or cell lysate from the value of said comparison result.

2. (Currently amended) ~~A method of screening a substance of interest for heme independent activation of soluble guanylyl cyclase comprising:~~

~~a) obtaining purified $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme or a cell lysate containing $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme;~~

~~b) assaying said purified enzyme or cell lysate for formation of cGMP from GTP in the presence of said substance;~~

~~c) assaying said purified enzyme or cell lysate for formation of cGMP from GTP in the absence of said substance;~~

~~d) optionally, carrying out steps b) and c) in the presence or absence of an activator other than said substance of interest; and~~

~~e) comparing the results from b) and c), and, d), if present, to determine whether~~ The method of claim 1 wherein the outcome of step f) indicates that said substance enhances cGMP production by said purified enzyme or cell lysate.

3. (Withdrawn) A method of identifying a functional region of soluble guanylyl cyclase that is responsible for sGC regulation comprising:

a) obtaining a library of deletion mutants of α subunit of soluble guanylyl cyclase;

b) producing mutant sGC enzymes containing β^{Cys105} subunit and α subunits with deletions obtained in step a);

c) obtaining cell lysates comprising the respective mutant sGC enzymes with α subunit deletions, from step b);

d) optionally, purifying said mutant sGC enzymes from step c);

e) assaying said purified enzymes or cell lysates from step c) or d) for formation of cGMP from GTP in the absence of activators or inhibitors;

f) assaying purified wild type sGC enzyme, or a cell lysate comprising said wild type sGC enzyme, for formation of cGMP from GTP in the absence of activators or inhibitors;

g) assaying purified $\alpha\beta^{Cys105}$ mutant sGC enzyme, or a cell lysate comprising said $\alpha\beta^{Cys105}$ sGC enzyme, for formation of cGMP from GTP in the absence of activators or inhibitors;

h) comparing the results from e) and f), and g) to determine whether any said α subunit deletion decreases or increases the activity of the corresponding mutant enzyme tested in step e), as compared to the $\alpha\beta^{Cys105}$ mutant sGC enzyme in step g), to levels comparable or identical to that of the wild type sGC enzyme in step f);

i) using the results of the comparison in step h), identifying an α subunit deletion mutant from step a) containing a deletion mutation that effects sGC activation.

4. (Withdrawn) The method of claim 3 wherein step i) comprises identifying an α subunit deletion mutant from step a) containing a deletion mutation that is critical for sGC activation.

5. (Withdrawn) A method to aid in identifying structural features of soluble guanylyl cyclase stimulation comprising

crystallizing purified $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme in the presence of DTT;

crystallizing purified $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase enzyme in the absence of DTT; and

comparing the resulting soluble guanylyl cyclase enzyme crystals, and

determining structural changes in the soluble guanylyl cyclase protein associated with the presence or absence of DTT.

6. (Withdrawn) A method of increasing and/or sustaining intracellular production of cyclic GMP in a mammalian cell comprising:

providing $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase, or the β^{Cys105} subunit thereof, to said cell, and/or

constitutively expressing in said cell of the $\alpha\beta^{Cys105}$ mutant soluble guanylyl cyclase gene, or a portion thereof containing at least the DNA coding for the β^{Cys105} subunit.

7-17. (Canceled)

18. (New) The method of claim 1 wherein the outcome of step f) indicates that said substance inhibits enhances cGMP production by said purified enzyme or cell lysate.

19. (New) The method of claim 18 wherein the outcome of step f) indicates that said substance affects a structural element of the sGC enzyme other than a heme moiety to cause inhibition of sGC activity.

20. (New) The method of claim 2 wherein the outcome of step f) indicates that said substance affects a structural element of the sGC enzyme other than a heme moiety to cause enhancement of sGC activity.

21. (New) The method of claim 1 wherein step d) is included and said activator comprises DTT.